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By: / Ruth Montalvo Date: 11/04/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Customer No.	026418		
Docket No.	JG-YY-5090 / 500569.20069	Group:	1634
Applicant(s):	Yoshihiko MAKINO, et al.		
Application No.:	09/887,625	Examiner:	A.K. CHAKRABARTI
Filed:	June 22, 2001		
For:	METHOD OF DETECTING NUCLEIC ACIDS		

Commissioner for Patents
Washington, D.C. 20231

AMENDMENT

Sir:

In response to the Office Action mailed May 3, 2002, please amend the above identified application as follows:

In the Claims

1. (amended) A method of detecting nucleic acid fragments in plural samples which comprises the steps of:

attaching an electroconductive label to nucleic acid fragments in o e sample and attaching another electroconductive label to nucleic acid fragments in another sample, the former electroconductive label and the latter electroconductive label having oxidation-reduction potentials differing from each other;

preparing a mixture of the samples containing nucleic acid fragments to which electroconductive labels are attached;

bringing the mixture into contact with an electroconductive microarray having plural electrodes onto which probe molecules complementary to the nucleic acid fragments are fixed, so that hybridization between the nucleic acid fragments having electroconductive labels and the probe molecules on the electroconductive microarray can proceed to form hybrid structures on the electrodes;

applying to the electrode an electric potential corresponding to the oxidation-reduction potential of the former electroconductive label and detecting on the electrode an electric current flowing along the hybrid structure;

and comparing the electric current detected in the former detecting procedure and the electric current detected in the latter detecting procedure to obtain a ratio of the content of the nucleic acid fragments in each sample.

REMARKS

Reconsideration and withdrawal of the rejection of the claims as being unpatentable under 35 USC 112 are respectfully requested. As a result of the foregoing amendment, claim 1 has been amended to recite that the comparing step provides a ratio of the content of the nucleic acid fragments in each sample. Clearly, there is no longer basis for the formal rejection raised by the Examiner and this rejection should be withdrawn.

Reconsideration and withdrawal of the rejection of claims 1-8 as being anticipated under 35 USC 102 (e) by the Mathies et al '671 are also respectfully requested. The examiner has asserted that Mathies et al teaches a method for detecting nucleic acid fragments in plural samples by first attaching an electroconductive label to a nucleic acid fragment in one sample and attaching another electroconductive label to fragments in another sample. The former and latter labels having oxidation reduction potentials differing from each other and then preparing a mixture of the samples to which the labels have been attached. Thereafter, the mixture is contacted with an electroconductive microarray having plural electrodes and to which probe molecules complimentary to the nucleic acid fragments are fixed so that hybridization between the nucleic acid fragments are fixed so that hybridization between the nucleic acid fragments having electroconductive labels and the probe molecules on the electroconductive microarray can proceed to form hybrid structures on the electrodes. Thereafter, an electric potential is applied to the electrode corresponding to the oxidation-reduction potential of the former electroconductive label and detecting on the electrode and electric current flowing along the hybrid structure and then applying an electric potential corresponding to the oxidation-reduction potential of the latter label and detecting an electric current flowing along the hybrid-structure on that electrode and thereafter comparing the electric currents detected between the former and the latter procedures. However, it is believed that the examiner's characterization of the third step (c) is inaccurate. The detection method of Mathies et al uses a microfabricated capillary electrophoresis chip for determining multiple redox-active labels simultaneously. The detection method comprises selectively labeling analytes for simultaneous electrochemical detection of multiple label-analyte conjugates after electrophoretic or chromatographic separation (see the abstract).

The prime difference between that the detection method disclosed in Mathies et al and that presently claimed is that in Mathies, the mixture of labeled samples is one separated from each other by electrophoretic or chromatographic separation and then electrochemically detected by an electrode system composed of a working electrode, a CE-ground electrode, a referencing electrode and an auxiliary electrode as depicted in Fig. 1. In contrast, in the present method as claimed, the mixture is directly brought into contact with a DNA chip which has a group of probe molecules thereon. The labeled samples in the mixture are hybridized with the probe molecules on the DNA chip and then the hybridized samples are detected electrochemically.

A careful review of the description in the Mathies reference and particularly that referred to by the Examiner, i.e., column 8, lines 55 to column 6, line 6; and column 10, lines 46-55 and Fig. 1. This confirms that there are no descriptions in the reference with respect to a DNA chip having a group of probe molecules nor is there any description of hybridization between the labeled DNA fragment and the probe molecules. Consequently, Mathies can not possibly anticipate the present invention as claimed and this rejection is untenable and should be withdrawn.

In view of the foregoing, it is submitted that this application is now in condition for allowance and favorable reconsideration and prompt notice of allowance are earnestly solicited.

Respectfully submitted,

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